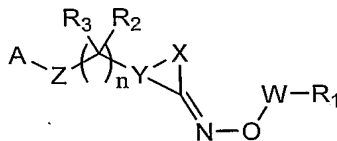


WE CLAIM

1. A compound of Formula I:



in which:

n is 0, 1 or 2;

R_1 is chosen from C_{6-10} aryl and C_{5-10} heteroaryl; wherein any aryl or heteroaryl of R_1 is optionally substituted by a radical chosen from C_{6-10} aryl C_{0-4} alkyl, C_{5-6} heteroaryl C_{0-4} alkyl, C_{3-8} cycloalkyl C_{0-4} alkyl, C_{3-8} heterocycloalkyl C_{0-4} alkyl or C_{1-10} alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R_1 can be optionally substituted by one to five radicals selected from the group consisting of halo, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy; and any alkyl group of R_1 can optionally have a methylene replaced by an atom or group chosen from $-S-$, $-S(O)-$, $-S(O)_2-$, $-NR_4-$ and $-O-$; wherein R_4 is chosen from hydrogen or C_{1-6} alkyl;

R_2 and R_3 are independently chosen from hydrogen, C_{1-6} alkyl, halo, hydroxy, C_{1-6} alkoxy, halo-substituted C_{1-6} alkyl and halo-substituted C_{1-6} alkoxy;

A is chosen from $-X_1C(O)OR_4$, $-X_1OP(O)(OR_4)_2$, $-X_1P(O)(OR_4)_2$, $-X_1P(O)OR_4$, $-X_1S(O)_2OR_4$, $-X_1P(O)(R_4)OR_4$ and $1H$ -tetrazol-5-yl; wherein X_1 is a bond or C_{1-6} alkylene and R_4 is chosen from hydrogen and C_{1-6} alkyl;

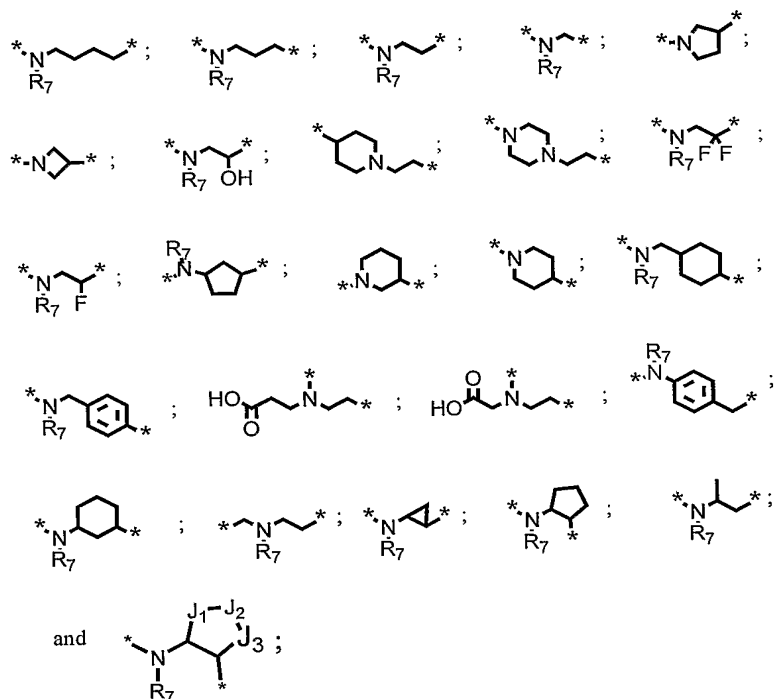
W is chosen from a bond, C_{1-6} alkylene and C_{2-6} alkenylene;

X is chosen from C_{2-4} alkylene and C_{2-4} alkenylene; wherein one methylene group of X can be replaced with an atom or group chosen from $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$ and $-NR_5-$; wherein R_5 is hydrogen, C_{1-6} alkyl and $-C(O)R_6$; wherein R_6 is chosen from hydrogen and C_{1-6} alkyl; wherein any alkylene or alkenylene of X can further be substituted by 1 to 3 radicals selected from the group consisting of halo, hydroxy, C_{1-6} alkyl, C_{1-6} alkoxy, halo-substituted C_{1-10} alkyl and halo-substituted C_{1-10} alkoxy;

Y is chosen from C₆₋₁₀aryl and C₅₋₁₀heteroaryl, wherein any aryl or heteroaryl of Y can be optionally substituted with 1 to 3 radicals chosen from halo, hydroxy, nitro, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted C₁₋₁₀alkyl and halo-substituted C₁₋₁₀alkoxy;

Z is C₁₋₆alkylene; wherein up to two methylene groups of Z can be replaced with divalent radicals chosen from -NR₇-. C₃₋₈cycloalkylene, C₃₋₈heterocycloalkylene and phenylene; wherein R₇ is chosen from hydrogen, C₁₋₆alkyl and (CH₂)₁₋₂COOH; wherein Z may further be substituted by 1 to 3 radicals chosen from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkoxy, halo-substitued-C₁₋₆alkyl and halo-substitued-C₁₋₆alkoxy; or when a -NR₇- replaces at least one methylene group of Z, R₇ and Y together with the nitrogen atom to which R₇ is attached, forms C₈₋₁₄heteroarylene; and the pharmaceutically acceptable salts, hydrates, solvates, isomers and prodrugs thereof.

2. The compound of claim 2 in which n is 0 or 1 and Z is chosen from:



wherein the left and right asterisks of Z indicate the point of attachment between the $-\text{[C(R}_2\text{)(R}_3\text{)]}_n-$ group and A of Formula I, respectively; R₇ is chosen from hydrogen and C₁₋₆alkyl; and J₁, J₂ and J₃ are independently methylene or a heteroatom selected from the group

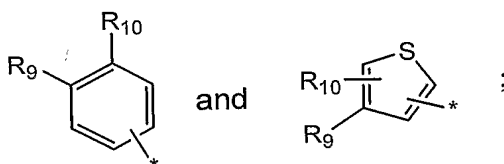
consisting of S, O and NR₄; wherein R₄ is hydrogen or C₁₋₆alkyl; with the proviso that the number of heteroatoms are 2 or less.

3. The compound of claim 1 in which R₁ is chosen from phenyl, naphthyl and thiophenyl optionally substituted by C₆₋₁₀arylC₀₋₄alkyl, C₅₋₆heteroarylC₀₋₄alkyl, C₃₋₈cycloalkylC₀₋₄alkyl, C₃₋₈heterocycloalkylC₀₋₄alkyl or C₁₋₁₀alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R₁ can be optionally substituted by 1 to 5 radicals chosen from halo, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted-C₁₋₁₀alkyl and halo-substituted-C₁₋₁₀alkoxy; and any alkyl group of R₁ can optionally have a methylene replaced by an atom or group chosen from -S-, -S(O)-, -S(O)₂-, -NR₄- and -O-; wherein R₄ is hydrogen or C₁₋₆alkyl.

4. The compound of claim 1 in which Y is chosen from phenyl, pyridine, pyrimidine, thiophene, furan, thiazole and oxazole; each of which can be optionally substituted with 1 to 3 radicals chosen from halo, hydroxy, nitro, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted C₁₋₁₀alkyl and halo-substituted C₁₋₁₀alkoxy.

5. The compound of claim 1 in which R₂ and R₃ are both hydrogen and A is chosen from -C(O)OR₄ and 1*H*-tetrazol-5-yl; wherein R₄ is chosen from hydrogen and C₁₋₆alkyl.

6. The compound of claim 1 in which R₁ is chosen from:



wherein the asterisk is the point of attachment of R₁ with W; R₉ is C₆₋₁₀arylC₀₋₄alkyl, C₅₋₆heteroarylC₀₋₄alkyl, C₃₋₈cycloalkylC₀₋₄alkyl, C₃₋₈heterocycloalkylC₀₋₄alkyl or C₁₋₁₀alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R₉ can be optionally substituted by 1 to 3 radicals chosen from halo, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-

substituted-C₁₋₁₀alkyl and halo-substituted-C₁₋₁₀alkoxy; and any alkyl group of R₉ can optionally have a methylene replaced by an atom or group chosen from -S-, -S(O)-, -S(O)₂-, -NR₄- and -O-; wherein R₄ is hydrogen or C₁₋₆alkyl; and R₁₀ is selected from halo, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted-C₁₋₁₀alkyl and halo-substituted-C₁₋₁₀alkoxy.

7. The compound of claim 1 chosen from: 3-{[5-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-5,6,7,8-tetrahydro-naphthalen-2-ylmethyl]-amino}-propionic acid; 1-[5-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-5,6,7,8-tetrahydro-naphthalen-2-ylmethyl]-azetidine-3-carboxylic acid; 3-{[6-chloro-4-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-chroman-7-ylmethyl]-amino}-propionic acid; 3-{[3-chloro-5-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-5,6,7,8-tetrahydro-naphthalen-2-ylmethyl]-amino}-propionic acid; 1-[3-Chloro-5-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-5,6,7,8-tetrahydro-naphthalen-2-ylmethyl]-azetidine-3-carboxylic acid; 1-[5-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-3-methoxy-5,6,7,8-tetrahydro-naphthalen-2-ylmethyl]-azetidine-3-carboxylic acid; 3-{[5-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-3-methoxy-5,6,7,8-tetrahydro-naphthalen-2-ylmethyl]-amino}-propionic acid; 3-{[8-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-5,6,7,8-tetrahydro-quinolin-3-ylmethyl]-amino}-propionic acid; 1-[8-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-5,6,7,8-tetrahydro-quinolin-3-ylmethyl]-azetidine-3-carboxylic acid; 3-{[4-[5-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-5,6,7,8-tetrahydro-naphthalen-2-yl]-piperazin-1-yl]-propionic acid; 3-{[1-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-indan-5-ylmethyl]-amino}-propionic acid; 1-[8-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-5,6,7,8-tetrahydro-naphthalen-2-ylmethyl]-azetidine-3-carboxylic acid; 3-{[8-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-5,6,7,8-tetrahydro-naphthalen-2-ylmethyl]-amino}-propionic acid; 3-{[5-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-3-ethyl-5,6,7,8-tetrahydro-naphthalen-2-ylmethyl]-amino}-propionic acid; 3-{[4-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-chroman-6-ylmethyl]-amino}-propionic acid; 3-{[4-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-chroman-7-ylmethyl]-amino}-propionic acid; 1-[4-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-chroman-7-ylmethyl]-azetidine-3-carboxylic acid; 3-{[4-(4-cyclohexyl-3-trifluoromethyl-benzyloxyimino)-3,4-dihydro-2H-pyrano[2,3-b]pyridin-7-ylmethyl]-amino}-propionic acid; 1-[4-(4-cyclohexyl-3-

trifluoromethyl-benzyloxyimino)-3,4-dihydro-2H-pyrano[2,3-b]pyridin-7-ylmethyl]-azetidine-3-carboxylic acid; 1-[4-(4-cyclohexyl-3-methyl-benzyloxyimino)-chroman-7-ylmethyl]-azetidine-3-carboxylic acid; and 3-{[4-(4-cyclohexyl-3-methyl-benzyloxyimino)-chroman-7-ylmethyl]-amino}-propionic acid.

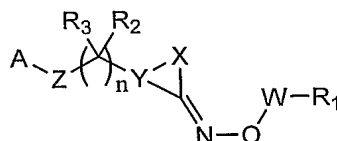
8. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in combination with a pharmaceutically acceptable excipient.

9. A method for treating a disease in an animal in which alteration of EDG/S1P receptor mediated signal transduction can prevent, inhibit or ameliorate the pathology and/or symptomology of the disease, which method comprises administering to the animal a therapeutically effective amount of a compound of Claim 1.

10. A method for preventing or treating disorders or diseases mediated by lymphocytes, for treating acute or chronic transplant rejection or T-cell mediated inflammatory or autoimmune diseases, for inhibiting or controlling deregulated angiogenesis, or for treating diseases mediated by a neo-angiogenesis process or associated with deregulated angiogenesis in a subject comprising administering to the subject in need thereof an effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof.

11. The use of a compound of claim 1 in the manufacture of a medicament for treating a disease in an animal in which alteration of EDG/S1P receptor mediated signal transduction contributes to the pathology and/or symptomology of the disease.

12. A process for preparing a compound of Formula I:



in which:

n is 0, 1 or 2;

R₁ is chosen from C₆₋₁₀aryl and C₅₋₁₀heteroaryl; wherein any aryl or heteroaryl of R₁ is optionally substituted by a radical chosen from C₆₋₁₀arylC₀₋₄alkyl, C₅₋₆heteroarylC₀₋₄alkyl, C₃₋₈cycloalkylC₀₋₄alkyl, C₃₋₈heterocycloalkylC₀₋₄alkyl or C₁₋₁₀alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R₁ can be optionally substituted by one to five radicals selected from the group consisting of halo, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted-C₁₋₁₀alkyl and halo-substituted-C₁₋₁₀alkoxy; and any alkyl group of R₁ can optionally have a methylene replaced by a member of the group consisting of -S-, -S(O)-, -S(O)₂-, -NR₄- and -O-; wherein R₄ is chosen from hydrogen or C₁₋₆alkyl;

R₂ and R₃ are independently chosen from hydrogen, C₁₋₆alkyl, halo, hydroxy, C₁₋₆alkoxy, halo-substituted C₁₋₆alkyl and halo-substituted C₁₋₆alkoxy;

A is chosen from -X₁C(O)OR₄, -X₁OP(O)(OR₄)₂, -X₁P(O)(OR₄)₂, -X₁P(O)OR₄, -X₁S(O)₂OR₄, -X₁P(O)(R₄)OR₄ and 1*H*-tetrazol-5-yl; wherein X₁ is a bond or C₁₋₆alkylene and R₄ is chosen from hydrogen and C₁₋₆alkyl;

W is chosen from a bond, C₁₋₆alkylene and C₂₋₆alkenylene;

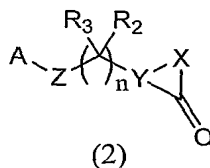
X is chosen from C₂₋₄alkylene and C₂₋₄alkenylene; wherein one methylene group of X can be replaced with an atom or group chosen from -O-, -S-, -S(O)-, -S(O)₂- and -NR₅-; wherein R₅ is hydrogen, C₁₋₆alkyl and -C(O)R₆; wherein R₆ is chosen from hydrogen and C₁₋₆alkyl; wherein any alkylene or alkenylene of X can further be substituted by 1 to 3 radicals selected from the group consisting of halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkoxy, halo-substituted C₁₋₁₀alkyl and halo-substituted C₁₋₁₀alkoxy;

Y is chosen from C₆₋₁₀aryl and C₅₋₁₀heteroaryl, wherein any aryl or heteroaryl of Y can be optionally substituted with 1 to 3 radicals chosen from halo, hydroxy, nitro, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted C₁₋₁₀alkyl and halo-substituted C₁₋₁₀alkoxy;

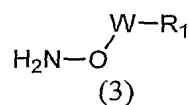
Z is C₁₋₆alkylene; wherein up to two methylene groups of Z can be replaced with divalent radicals chosen from -NR₇-, C₃₋₈cycloalkylene, C₃₋₈heterocycloalkylene and phenylene; wherein R₇ is chosen from hydrogen, C₁₋₆alkyl and (CH₂)₁₋₂COOH; wherein Z may further be substituted by 1 to 3 radicals chosen from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkoxy, halo-substituted-C₁₋₆alkyl and halo-substituted-C₁₋₆alkoxy; or when a -NR₇- replaces

at least one methylene group of Z, R₇ and Y together with the nitrogen atom to which R₇ is attached, forms C₈₋₁₄heteroarylene; which process comprises:

- (a) reacting a compound of formula 2:



with a compound of formula 3:

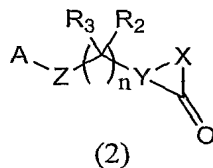


in which A, W, X, Y, Z, R₁, R₂, R₃ and n are as defined for Formula I above; and

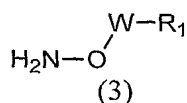
- (b) optionally converting a compound of the invention into a pharmaceutically acceptable salt;
- (c) optionally converting a salt form of a compound of the invention to a non-salt form;
- (d) optionally converting an unoxidized form of a compound of the invention into a pharmaceutically acceptable N-oxide;
- (e) optionally converting an N-oxide form of a compound of the invention to its unoxidized form;
- (f) optionally resolving an individual isomer of a compound of the invention from a mixture of isomers;
- (g) optionally converting a non-derivatized compound of the invention into a pharmaceutically acceptable prodrug derivative; and
- (h) optionally converting a prodrug derivative of a compound of the invention to its non-derivatized form.

at least one methylene group of Z, R₇ and Y together with the nitrogen atom to which R₇ is attached, forms C₈₋₁₄heteroarylene; which process comprises:

- (a) reacting a compound of formula 2:



with a compound of formula 3:

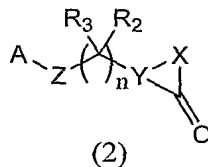


in which A, W, X, Y, Z, R₁, R₂, R₃ and n are as defined for Formula I above; and

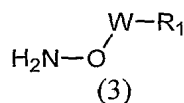
- (b) optionally converting a compound of the invention into a pharmaceutically acceptable salt;
- (c) optionally converting a salt form of a compound of the invention to a non-salt form;
- (d) optionally converting an unoxidized form of a compound of the invention into a pharmaceutically acceptable N-oxide;
- (e) optionally converting an N-oxide form of a compound of the invention to its unoxidized form;
- (f) optionally resolving an individual isomer of a compound of the invention from a mixture of isomers;
- (g) optionally converting a non-derivatized compound of the invention into a pharmaceutically acceptable prodrug derivative; and
- (h) optionally converting a prodrug derivative of a compound of the invention to its non-derivatized form.

at least one methylene group of Z, R₇ and Y together with the nitrogen atom to which R₇ is attached, forms C₈₋₁₄heteroarylene; which process comprises:

(a) reacting a compound of formula 2:



with a compound of formula 3:

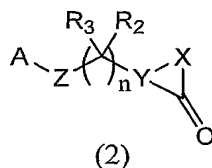


in which A, W, X, Y, Z, R₁, R₂, R₃ and n are as defined for Formula I above; and

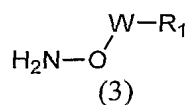
- (b) optionally converting a compound of the invention into a pharmaceutically acceptable salt;
- (c) optionally converting a salt form of a compound of the invention to a non-salt form;
- (d) optionally converting an unoxidized form of a compound of the invention into a pharmaceutically acceptable N-oxide;
- (e) optionally converting an N-oxide form of a compound of the invention to its unoxidized form;
- (f) optionally resolving an individual isomer of a compound of the invention from a mixture of isomers;
- (g) optionally converting a non-derivatized compound of the invention into a pharmaceutically acceptable prodrug derivative; and
- (h) optionally converting a prodrug derivative of a compound of the invention to its non-derivatized form.

at least one methylene group of Z, R₇ and Y together with the nitrogen atom to which R₇ is attached, forms C₈₋₁₄heteroarylene; which process comprises:

- (a) reacting a compound of formula 2:



with a compound of formula 3:



in which A, W, X, Y, Z, R₁, R₂, R₃ and n are as defined for Formula I above; and

- (b) optionally converting a compound of the invention into a pharmaceutically acceptable salt;
- (c) optionally converting a salt form of a compound of the invention to a non-salt form;
- (d) optionally converting an unoxidized form of a compound of the invention into a pharmaceutically acceptable N-oxide;
- (e) optionally converting an N-oxide form of a compound of the invention to its unoxidized form;
- (f) optionally resolving an individual isomer of a compound of the invention from a mixture of isomers;
- (g) optionally converting a non-derivatized compound of the invention into a pharmaceutically acceptable prodrug derivative; and
- (h) optionally converting a prodrug derivative of a compound of the invention to its non-derivatized form.